**DOCKET NO.:** ISIS-5031 **Application No.:** 10/087,424

Office Action Dated: September 29, 2003

PATENT REPLY FILED UNDER EXPEDITED PROCEDURE PURSUANT TO 37 CFR § 1.116

## **REMARKS/ARGUMENTS**

The present invention is directed to a novel method for making a library of compounds from a purine or pyrimidine heterocyclic scaffold (see for example, page 2, lines 25-34 and page 6, lines 3-15). The method of the instant invention contacts a purine or pyrimidine heterocyclic scaffold having at least two functionalizable atoms, at least one of which is blocked, with a mixture of chemical substituents to append each of the chemical substituents to the heterocyclic scaffold directly to form a substituent-appended scaffold (page 2, lines 25-34 and page 10, lines 9-29). Next, at least one of the blocked functionalizable atoms is deblocked and contacted with a mixture of chemical substituents to append each of the chemical substituents to the substituent-appended scaffold (*Id.*). The method of the instant claims allows for solution phase production of the library of compounds in a single reaction vessel (page 2, lines 11-23).

Claims 31-50 are pending. No claims are added, amended, or canceled. All claims are under Final Rejection. As discussed in detail below, Applicants traverse all rejections.

Claims 31-50 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly exceeding the scope of the disclosure. Applicants traverse this rejection. The Office Action alleges that the examples do not "represent a *substantial* portion of the claimed genus" and that the claims are directed to "a virtually unlimited number of compounds" (Office Action at page 3). As pointed out by the Office Action, however, the requirement is the use of *representative* examples to provide reasonable assurance that the applicant had possession of the claimed invention at the time of filing (the paragraph spanning pages 3-4). The instant specification and its 117 examples easily meet the *representative* examples standard required to show one skilled in the art that Applicants were in possession of the invention at the time of filing.

Applicant has shown possession of the claimed invention by describing the claimed invention with its limitations using such descriptive means as words, structures, diagrams, and formulas that fully set forth the claimed invention. See Lockwood v. American Airlines, Inc., 107 F.3d 1656, 1572 (Fed. Cir. 1997). There is a strong presumption that an adequate written description of the claimed invention is present when the application is filed. See In re Wertheim, 541 F.2d 257, 263 (C.C.P.A. 1976). The heterocyclic scaffolds and substituents

**DOCKET NO.:** ISIS-5031 **Application No.:** 10/087,424

Office Action Dated: September 29, 2003

PATENT REPLY FILED UNDER EXPEDITED PROCEDURE PURSUANT TO 37 CFR § 1.116

are described, for example, in words at page 10, line 9 to page 15, line 31 and in the 117 examples, and further by the schematics shown on pages 27-55. These "words, structures, diagrams, and formulas" fully set forth the claimed invention. Thus, the disclosure clearly shows that Applicants were in possession of the subject matter of the instant claims.

Furthermore, Applicants dispute the assertion that the claims are directed to "a virtually unlimited number of compounds." The instant claims are directed to methods concerning a circumscribed and properly defined set of purine and pyrimidine heterocyclic scaffolds. These scaffolds are limited to those that have at least two functionalizable atoms. The functionizable atoms can only be at a limited number of positions on the claimed small molecule scaffolds. As understood by one skilled in the art, the functionalizable atoms are not of unlimited scope. Such atoms are described in the specification at, for example, page 7, line 29 to page 8, line 12. Thus, the claims are not of unlimited scope and are supported by significant description including 117 representative examples. As such, Applicants assert that the rejection is improper and withdrawal of the rejection is respectfully requested.

Claims 31, 32, 34-36, 38, 39, 41-43, and 45-49 stand rejected under 35 U.S.C. § 102(a) as allegedly anticipated by PCT Patent Application No. WO 96.33972 (the Gordeev reference). A reference cannot anticipate a claim, however, unless it discloses "every element as set forth in the claim . . . either expressly or inherently described." *Verdegaal Bros. v. Union Oil Co. of Calif.*, 814 F.2d 628, 631 (Fed. Cir. 1987); MPEP § 2131. "The identical invention must be shown in as complete detail as is contained in the . . . claim." *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236 (Fed. Cir. 1989); MPEP § 2131. The Gordeev reference falls short of this standard.

The Gordeev reference discloses a significantly different method than the method of the instant claims. Instant claim 31 is directed to a method of preparing a library of compounds starting with a purine or pyrimidine heterocyclic scaffold having at least two functionalizable atoms, at least one of which is blocked. The scaffold is reacted with a mixture of chemical substituents. At least one blocking group is then removed from the substituted scaffold, and the deblocked scaffold is reacted with a mixture of chemical substituents to produce the library of compounds. The method taught by the Gordeev reference differs considerably in that it takes a mixture of amino acid precursors and reacts them to produce their respective guanidine derivatives (see the Summary of the Invention on

**DOCKET NO.:** ISIS-5031 **Application No.:** 10/087,424

Office Action Dated: September 29, 2003

PATENT REPLY FILED UNDER EXPEDITED PROCEDURE PURSUANT TO 37 CFR § 1.116

pages 7-16 and pages 81-84). The products in Gordeev, in contrast to the instant claims, are not produced by reacting the functionalized purine or pyrimidine scaffold with a mixture of chemical substitutents but rather by reacting functionized precursors to produce the already substituted product (see pages 81-85 and Figure 10, for example). Thus, the method of Gordeev does not anticipate the instant claims.

Furthermore, the Office Action (page 7) mistakenly asserts that the instant claims do not require "beginning with a fully formed purine or pyrimidine scaffold and appending substitutents thereto." In instant claim 31, step a recites "contacting a purine or pyrimidine heterocyclic scaffold...." This reflects a fully formed scaffold. Subsequent language describes appending substitutents thereto. Clearly the Office Action's assertion is incorrect. Moreover, Applicants disagree with the Office Action's assessment of the importance of the use of the "comprising" transition phrase. Even though the comprising language does allow for additional steps, the instant claims still require appending substitutents to the heterocyclic scaffold. This is not taught by the Gordeev reference.

The foregoing arguments apply equally to independent claims 39 and 45 and the pending dependent claims. For at least these reasons, the Gordeev reference does not anticipate any instant claim. Applicants respectfully request reconsideration and withdrawal of § 102(a) rejections.

Claims 31-50 are rejected under 35 U.S.C. § 103(a) as allegedly obvious over the Gordeev reference and Bioorg. Med. Chem. Lett. 1994, 4, 2821-24 (the Smith reference). As discussed above the Gordeev reference lacks elements of each rejected claim. Nothing in the Smith reference overcomes, or is alleged to overcome, these deficiencies. As such, Applicants respectfully request reconsideration and withdrawal of the rejection.

**DOCKET NO.:** ISIS-5031 **Application No.:** 10/087,424

Office Action Dated: September 29, 2003

PATENT REPLY FILED UNDER EXPEDITED PROCEDURE PURSUANT TO 37 CFR § 1.116

Applicants believe that the claims presently before the Examiner patentably define the invention over the art of record and are otherwise in condition for ready allowance. An early Office Action to that effect is, therefore, earnestly solicited.

Respectfully submitted,

Date: November 25, 2003

John A. Harrelson, Jr. Registration No. 42,637

Woodcock Washburn LLP One Liberty Place - 46th Floor Philadelphia PA 19103 Telephone: (215) 568-3100

Facsimile: (215) 568-3439